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13. ABSTRACT This report lists twelve publications concerning synthesis and properties of bicyclic small ring compounds. It also discusses unpublished work and work that is presently being published including (1) Wurtz reactions of bridgehead-bridgehead dihalides, (2) bicyclo (2.2.0) hexene, (3) trans-fused bicyclo (n.1.0) alkanes, and (4) other bicyclic compounds.		
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Final Technical Report to the U.S. Army Research Office

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Name of Institution: Yale University, New Haven, Conn.

Principal Investigator: Kenneth B. Wiberg

Manuscripts published under ARO-D sponsorship:

"Heats of Formation of C_4H_6 Hydrocarbons", K. B. Wiberg and R. A. Fenoglio, J. Am. Chem. Soc., 90, 3395 (1968)

"Distorted Geometries about Bridgehead Carbons", K. B. Wiberg, J. E. Hiatt and G. Burgmaier, *Tetrahedron Letters*, 5855 (1968)

"trans-Bicyclo[5.1.0]octane", K. B. Wiberg and A. de Meijere, Tetrahedron Letters, 519 (1969).

"cis and trans-Bicyclo[6.1.0]nonan-2,3 and 4-ones", K. B. Wiberg and A. de Meijere, *Tetrahedron Letters*, 59, 1969).

"Tricyclo[3.2.1.0]octane", K. B. Wiberg and G. J. Burgmaier, Tetrahedron Letters, 317 (1969).

"trans-Bicyclo[5.1.0]octane", K. B. Wiberg and A. deMeijere, Tetrahedron Letters, 519 (1969).

"Tricyclo[3.2.1.0]octane and 8-Oxatricyclo[3.2.1.0]octane. Heat of Formation, Strain Energy and Reactivity", K. B. Wiberg, E. C. Lupton, Jr. and G. J. Burgmaier, J. Am. Chem. Soc., 91, 3372 (1969).

"Nuclear Magnetic Resonance Spectra of endo-Bicyclo[2.1.0]-pentan-2-ol, Cyclobutanol and cis-1,3-Dibromobutane", K. B. Wiberg and D. E. Barth. J. Am. Chem. Soc. 91, 5124 (1969).

"Bicyclo[1.1.1]pentane Derivatives", K. B. Wiberg and V. Z. Williams, Jr., J. Org. Chem., 35, 369(1970).

"Solvolysis of Bicyclo[2.1.1]hexyl-5 and Bicyclo[1.1.1]pentyl-2 Derivatives", K. B. Wiberg, R. A. Fenoglio, V. Z. Williams, Jr., and R. W. Ubersax, J. Am. Chem. Soc., 92, 568 (1970).

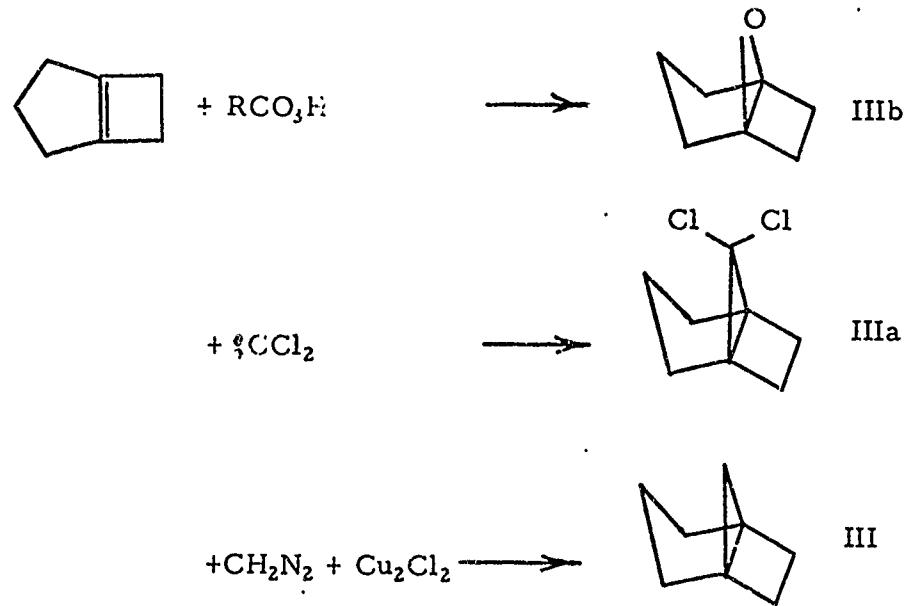
"Acid Catalyzed Solvolyses of Bicyclobutane Derivatives. Stereochemistry of the Cyclopropylcarbinyl-Cyclopropylcarbinyl and related Rearrangements", K. B. Wiberg and G. Szeimies, J. Am. Chem. Soc., 92, 571 (1970).

" Δ^{14} -Bicyclo[2.2.0]hexene", K. B. Wiberg, G. J. Burgmaier and P. Warner, J. Am. Chem. Soc., 93, 246 (1971).

3.

Summary of work carried out during the grant period. This covers mainly the still unpublished work, or that which is in press.

1. Tricyclo[3.2.1.0^{2,5}]octane (III). The report by Kirmse and Pook⁶ of the synthesis of $\Delta^{1,5}$ -bicyclo[3.2.0]heptene made it interesting to consider the synthesis of III. The hydrocarbon and its derivatives proved to be easily prepared as shown below.³

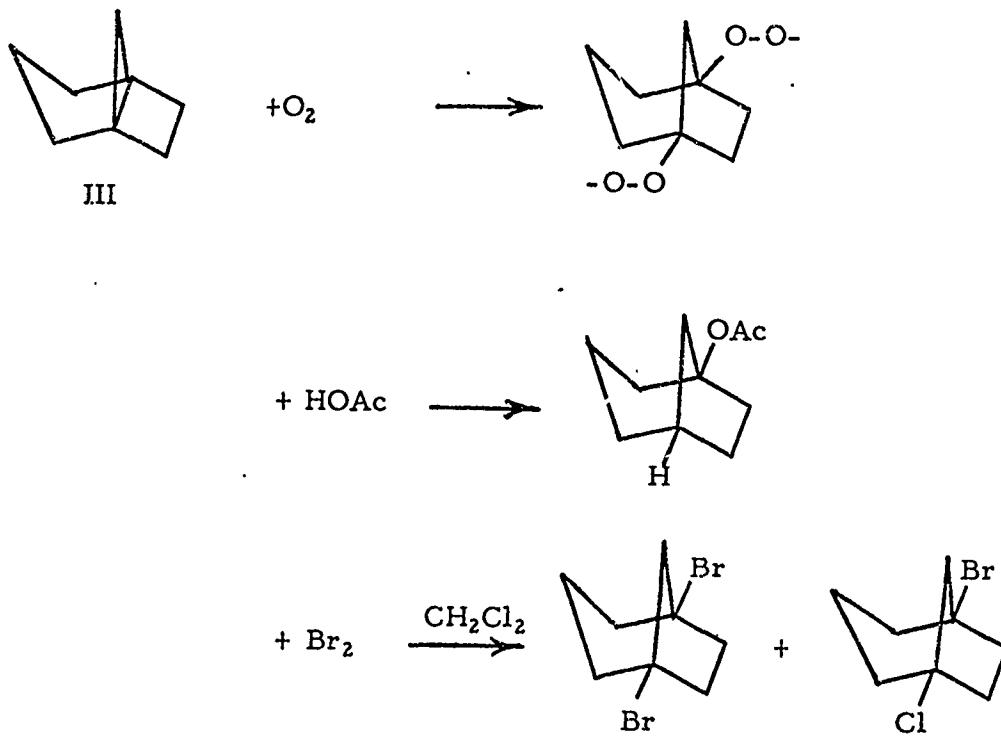


On the basis of molecular models, we concluded that these compounds should possess an "inverted" tetrahedral geometry at the bridgehead. Thus, if one were to pass a plane through the three CH_2 groups attached to a given bridgehead carbon, the plane should intersect the central C-C bond. Subsequent electron diffraction studies of III and IIIb,⁷

as well as an X-ray crystallographic study of IIIa⁸ have indicated that this conclusion is correct. As indicated in the introduction, the only reasonable hybridization at the bridgehead is approximately sp^2 to the CH_2 groups and p to the other bridgehead carbon.

The thermolysis of III was investigated, and it was found to have a half-life of about 20 hours at 200°. The product was a saturated polymer which did not appear to be derived from any olefinic rearrangement product, but rather appeared to be formed via intermolecular bridgehead-bridgehead coupling. The thermal stability of III, despite its considerable strain, is probably a consequence of the geometry which prohibits a symmetry allowed two step cleavage of the cyclobutane ring and prohibits the formation of products having a double bond to the bridgehead.

On the other hand, III is quite reactive toward other reagents. Thus, it reacts readily with oxygen at room temperature to give a 1:1 copolymer with an average molecular weight of 1700. It reacts essentially instantaneously with acetic acid and also with halogens. The latter reaction is interesting in that the intermediate organic radical is quite reactive and abstracts a chlorine from methylene chloride.



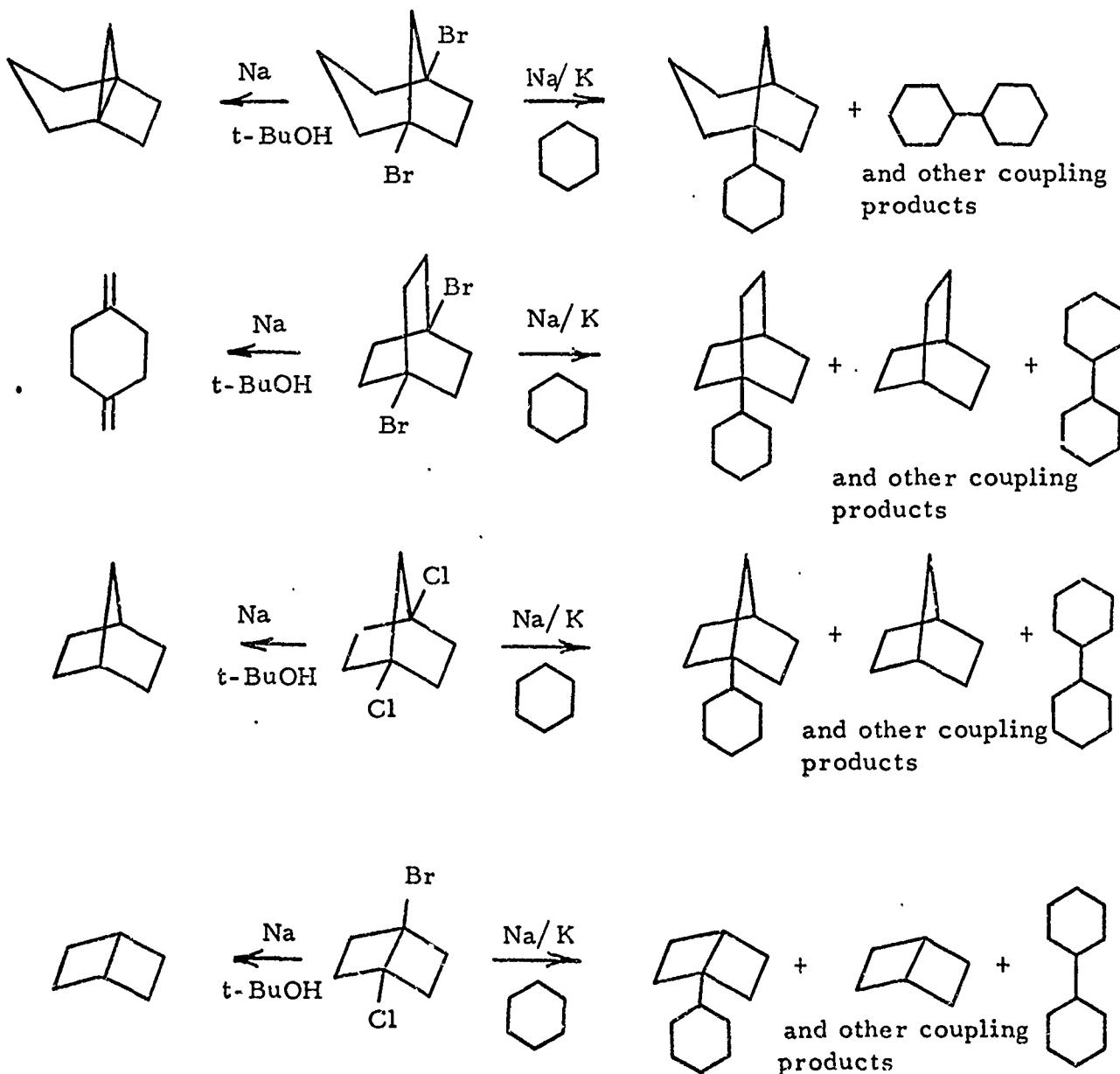
The hydrocarbon, III, also reacts readily with a number of other reagents such as acetylenedicarboxylic ester and bromotrichloromethane.

The heat of combustion of III could not readily be determined because of its high reactivity. However, the epoxide, IIIb, does not react with oxygen. Its heat of combustion was determined and led to a strain energy of 65 kcal/mole.⁹ This is not very much higher than that of bicyclo[2.1.0]pentane (53 kcal/mole), suggesting that it may be possible to prepare compounds of this type having smaller rings.

2. Wurtz Reactions of Bridgehead-bridgehead Dihalides. One of the possible ways by which tricyclo[2.2.2.0^{1,4}]octane (IX) and

tricyclo[2.2.1.0^{1,4}]heptane (VIII) might be prepared via a Wurtz reaction of the corresponding bridgehead-bridgehead dihalides. This type of reaction has proven very useful for the synthesis of bicyclobutane¹ and of bicyclo[1.1.1]pentane.²

The dihalides were prepared by conventional methods and were subjected to Wurtz type conditions with the following results:



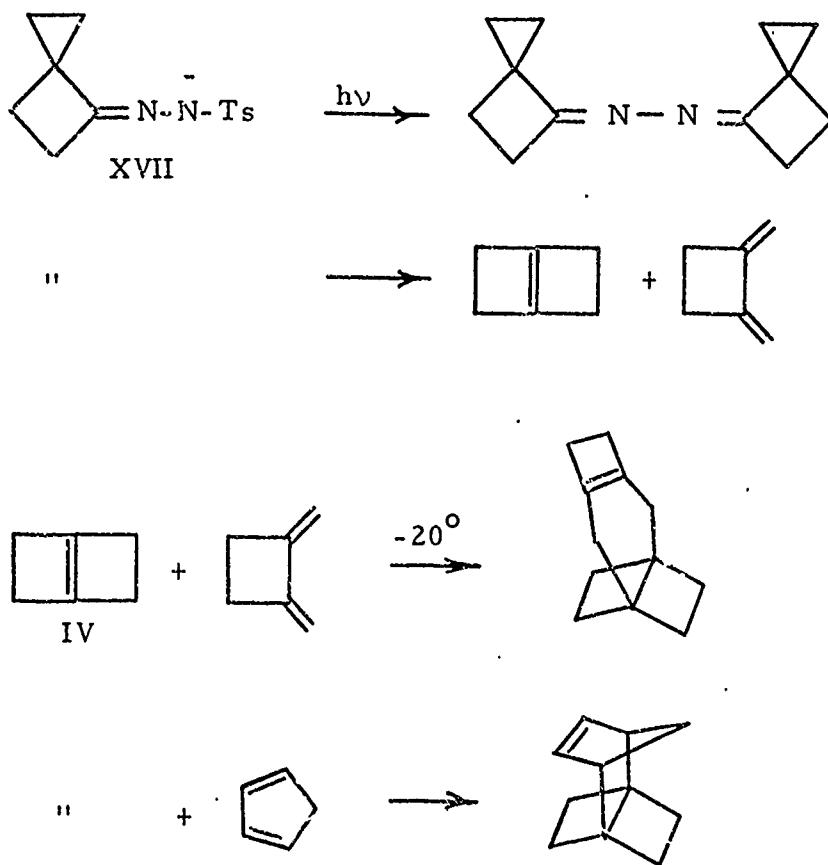
The Wurtz reactions carried out in cyclohexane as the solvent were uniformly unsuccessful; and gave predominantly free radical coupling products. In a better ionizing solvent, and particularly under dissolving metal conditions, XIII gave the hydrocarbon III as the only volatile product. However, XIV gave mainly the Grob type fragmentation product, 1, 4-dimethylcyclohexane, whereas XV and XVI underwent only reduction. The Wurtz reaction therefore appears unsuited to the preparation of the desired tricyclic compounds and $\Delta^{1,4}$ -bicyclo-[2.2.0]hexene.

3. $\Delta^{1,4}$ -Bicyclo[2.2.0]hexene. With the failure of the Wurtz closures, $\Delta^{1,4}$ -bicyclo[2.2.0]hexene (IV) became the key intermediate for attempted synthesis of VIII and IX. The alkene, IV, is also interesting in its own right. A number of attempts were made to prepare IV. One method, from the dihalide, was unsuccessful as indicated above. Other methods of dehalogenating XVI (such as with sodium phenanthrene radical anion) were equally unsuccessful.

This led us to examine the possibility of preparing IV via the diazoalkane as Kirmse and Pook⁶ had done for the next higher homolog. The photolysis of the tosylhydrazone XVII was not successful and gave only the azene.³ The thermolysis of XVII was however found to be satisfactory provided it was carried out under high vacuum and the product collected in a liquid nitrogen cooled trap.¹⁰

When the contents of the trap were allowed to warm to 0°,

an exothermic reaction occurred leading to a Diels-Alder adduct between IV and 1,2-dimethylenecyclobutane which is also formed in the reaction. The addition of an excess of cyclopentadiene before warming the contents of the trap led to the Diels-Alder adduct between IV and cyclopentadiene.



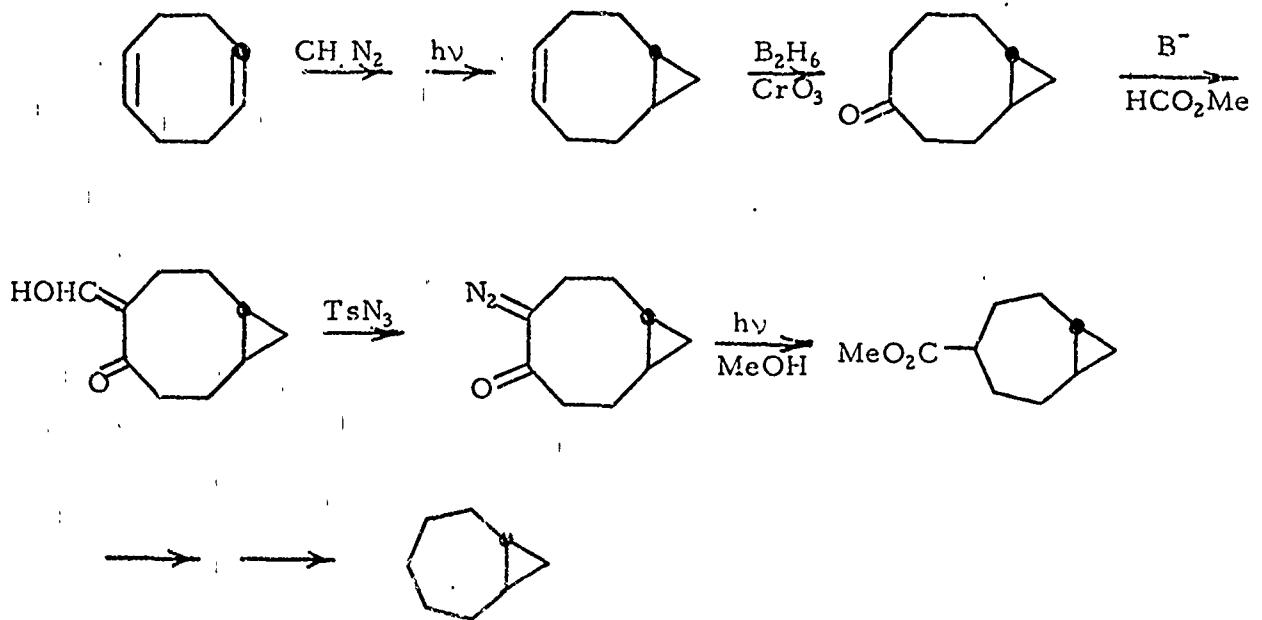
The nmr spectrum of IV could be obtained at low temperature.

3. Trans-fused Bicyclo[n.1.0]alkanes. We have prepared both cis and trans-fused bicyclo[6.1.0]nonanes and have determined

both their heats of combustion and reactivity toward acetic acid.⁵

Both were found to have the same heat of combustion indicating no difference in strain energy.¹¹ This is in contrast to the cis- and trans-cyclooctenes which differ in energy by 9 kcal/mole.¹² The reactivity towards acetic acid was found to be essentially the same, and the same type of products were formed in both cases.

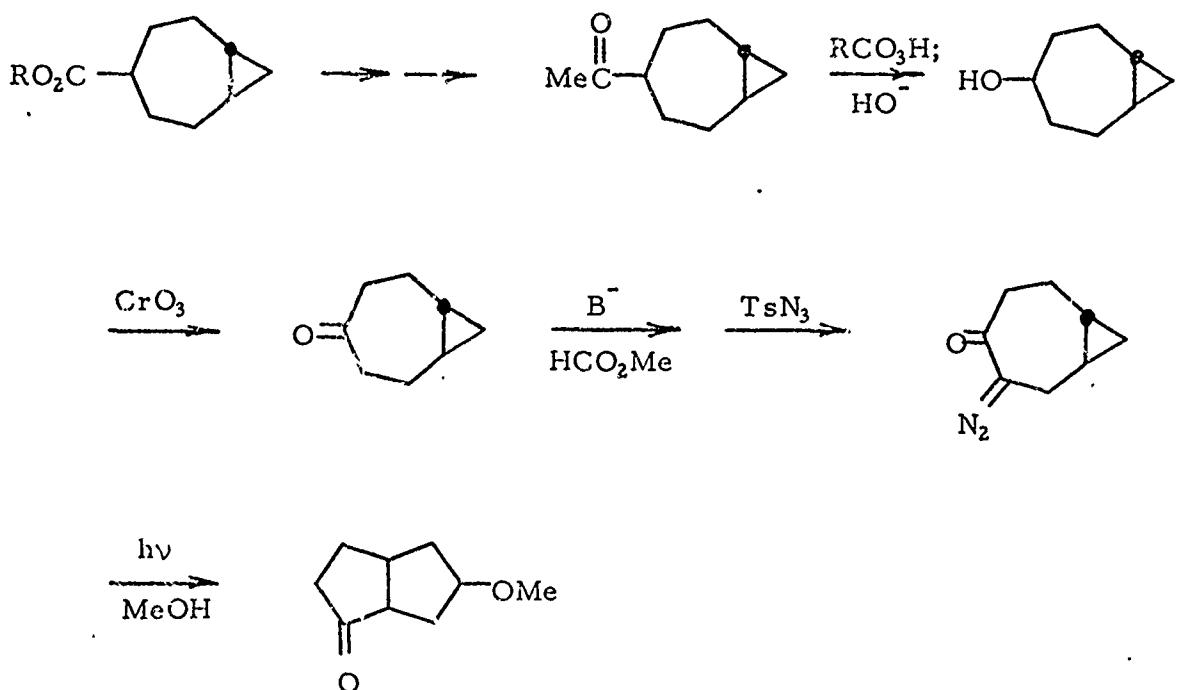
The trans-fused bicyclo[5.1.0]octane was prepared by the sequence:



The hydrocarbon was found to be 18X as reactive toward acetic acid as the bicyclo[6.1.0]nonanes, and the predominant mode of bond cleavage involved the central bond in contrast to most other compounds in this series. This indicates a small but significant destabilization of the central bond by trans-ring fusion.

An attempt was made to prepare the next smaller compound by

a second ring contraction as follows:



The formation of the α -formylketone was difficult because the ketone was resistant to enolization. Nevertheless, it was possible to effect the conversion, and the reaction with tosyl azide proceeded normally. However, in the photolysis step an abnormal reaction occurred leading to a bicyclo[3.3.0]octane derivative.

4. Other Bicyclic Compounds. We have examined the preparation and interconversion of bicyclo[1.1.1]pentane derivatives in some detail. The results of this investigation have been published.² The 1-substituted derivatives are fairly easily prepared, but the 2-substituted compounds are still not readily obtained either by our procedure or those of others.¹³

We have examined the preparation of bicyclo[2.1.1]hexen-5-yl derivatives, and the results of this investigation have in part been

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published.¹⁴ The compound of major interest, endo-bicyclo[2.1.1]-hex-2-en-5-ol, could not be obtained because of its very ready rearrangement to benzene. The details of the transformations are being prepared for publication.

5. NMR Studies. One of the most important techniques in investigating the structure of the compounds described above has been nmr spectroscopy. In order to learn more about the effect of geometry on coupling constants and of substituents on chemical shifts, we have begun a detailed investigation of the spectra of some of the compounds. The spectra of twenty-two monosubstituted cyclopropanes have been completely analyzed, and the spectra of four monosubstituted cyclobutanes have also been completely analyzed.⁵ The spectra of a series of bicyclo[1.1.1]pentane and bicyclo[2.1.1]hexane derivatives are being studied in order to provide a series of compounds with known fixed relationships between substituents and C-H bonds. This will permit a detailed theoretical examination of the relation between the chemical shift and the geometry and nature of the substituent.

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